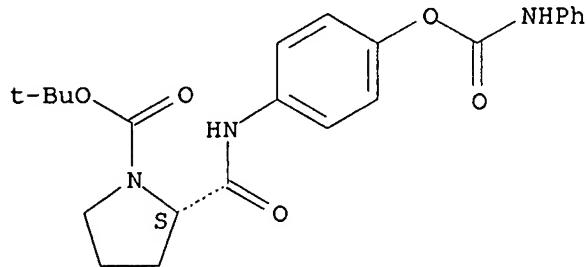


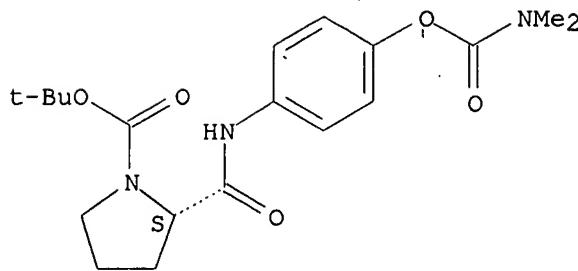
L9 ANSWER 4 OF 6 CAPIUS COPYRIGHT 2002 ACS  
 AN 1986:460932 CAPIUS  
 DN 105:60932  
 TI Peptidyl carbamates incorporating amino acid isosteres as novel elastase inhibitors  
 AU Digenis, George A.; Agha, Bushra J.; Tsuji, Kiyoshi; Kato, Masayuki; Shinogi, Masaki  
 CS Coll. Pharm., Univ. Kentucky, Lexington, KY, 40536-0053, USA  
 SO J. Med. Chem. (1986), 29(8), 1468-76  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DT Journal  
 LA English  
 OS CASREACT 105:60932  
 AB Title peptidyl carbamates  $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{CO-Ala-Ala-Pro-NHZO}_2\text{CNRR}_1$  [I; Z = p-C<sub>6</sub>H<sub>4</sub>, R = H, R<sub>1</sub> = Ph, CHMe<sub>2</sub>; Z = p-C<sub>6</sub>H<sub>4</sub>, R = R<sub>1</sub> = Me; Z = o-C<sub>6</sub>H<sub>4</sub>, CH(CHMe<sub>2</sub>)CH<sub>2</sub>, R = H, R<sub>1</sub> = Ph] and  $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{CO-Ala-Ala-Pro-CH}_2\text{N}(\text{CHMe}_2)\text{COXR}_2$  [II; X = O, R<sub>2</sub> = C<sub>6</sub>H<sub>4</sub>NO<sub>2</sub>-p, Ph, C<sub>6</sub>F<sub>5</sub>, CH<sub>2</sub>CF<sub>2</sub>CF<sub>2</sub>CF<sub>3</sub>; X = S, R<sub>2</sub> = CH<sub>2</sub>Ph, 1-methyl-5-tetrazolyl, 1-phenyl-5-tetrazolyl] were prepd. and they were tested as inhibitors of elastase, trypsin, and chymotrypsin. Thus, Boc-Pro-NHZOH (Boc = Me<sub>3</sub>CO<sub>2</sub>C) were treated with RR<sub>1</sub>NCOCl or RR<sub>1</sub>NCO to give Boc-Pro-NHZO<sub>2</sub>CNRR<sub>1</sub>, which were Boc-deblocked and then coupled with  $\text{MeO}_2\text{CCH}_2\text{CH}_2\text{CO-Ala-Ala-OH}$  (III) by ClCO<sub>2</sub>CH<sub>2</sub>CHMe<sub>2</sub> to give I. Boc-Pro-CH<sub>2</sub>Cl was treated with H<sub>2</sub>NCHMe<sub>2</sub> to give Boc-Pro-CH<sub>2</sub>NHCHMe<sub>2</sub>, which was treated with R<sub>2</sub>XCOCl to give Boc-Pro-CH<sub>2</sub>N(CHMe<sub>2</sub>)COXR<sub>2</sub>, which were Boc-deblocked and then coupled with III to give II. Six peptidyl carbamates specifically inhibited elastase without affecting trypsin and chymotrypsin. Kinetic studies showed that the inhibition was competitive. The inhibition is reversible and proceeds via the rapid formation of a strong enzyme-inhibitor complex, followed by slow acylation of the serine residue on the active site of the enzyme.  
 IT 102284-31-1P 102284-32-2P 102284-33-3P  
**102284-34-4P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and deblocking of)  
 RN 102284-31-1 CAPIUS  
 CN 1-Pyrrolidinecarboxylic acid, 2-[[[4-[[[(phenylamino)carbonyl]oxy]phenyl]amino]carbonyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 102284-32-2 CAPIUS  
 CN 1-Pyrrolidinecarboxylic acid, 2-[[[4-[[[(dimethylamino)carbonyl]oxy]phenyl]amino]carbonyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

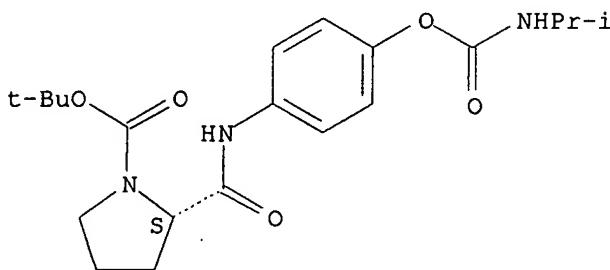
Absolute stereochemistry.



RN 102284-33-3 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 2-[[[4-[(1-methylethyl)amino]carbonyl]oxy]phenyl]amino]carbonyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

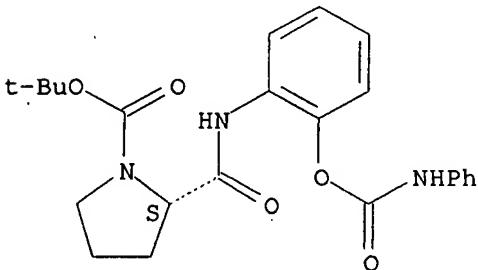
Absolute stereochemistry.



RN 102284-34-4 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 2-[[[2-[(phenylamino)carbonyl]oxy]phenyl]amino]carbonyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 102284-36-6P 102284-37-7P 102284-38-8P

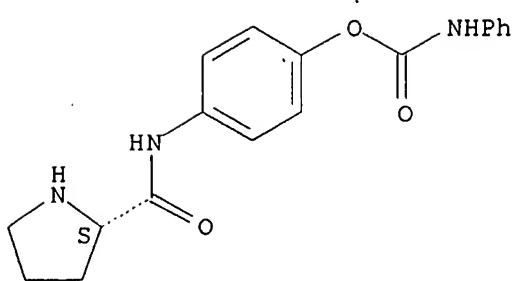
102284-39-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and peptide coupling of, with (methoxycarbonyl)propionyl  
dipeptide)

RN 102284-36-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, N-[4-[(phenylamino)carbonyl]oxy]phenyl]-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

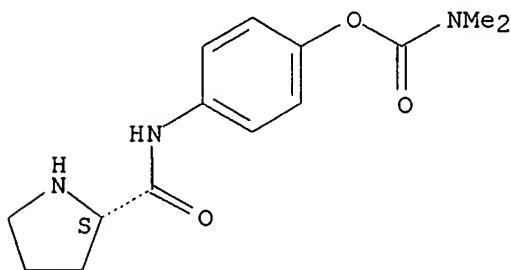


● HCl

RN 102284-37-7 CAPLUS

CN Carbamic acid, dimethyl-, 4-[(2-pyrrolidinylcarbonyl)amino]phenyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

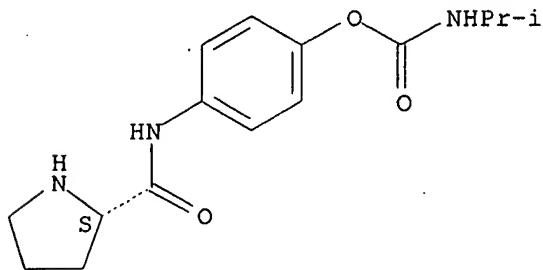


● HCl

RN 102284-38-8 CAPLUS

CN Carbamic acid, (1-methylethyl)-, 4-[(2-pyrrolidinylcarbonyl)amino]phenyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

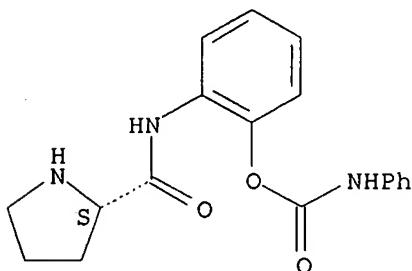


● HCl

RN 102284-39-9 CAPLUS

CN 2-Pyrrolidinecarboxamide, N-[2-[(phenylamino)carbonyl]oxy]phenyl-,  
monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT 92279-27-1P 92279-28-2P 92279-29-3P

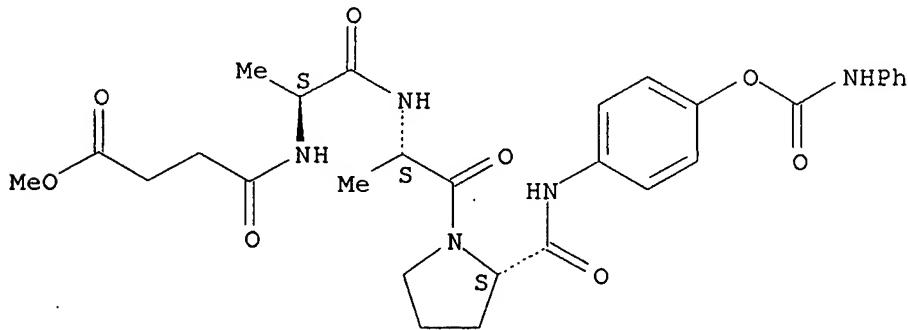
92279-30-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 92279-27-1 CAPLUS

CN L-Prolinamide, N-(4-methoxy-1,4-dioxobutyl)-L-alanyl-L-alanyl-N-[4-  
[(phenylamino)carbonyl]oxy]phenyl- (9CI) (CA INDEX NAME)

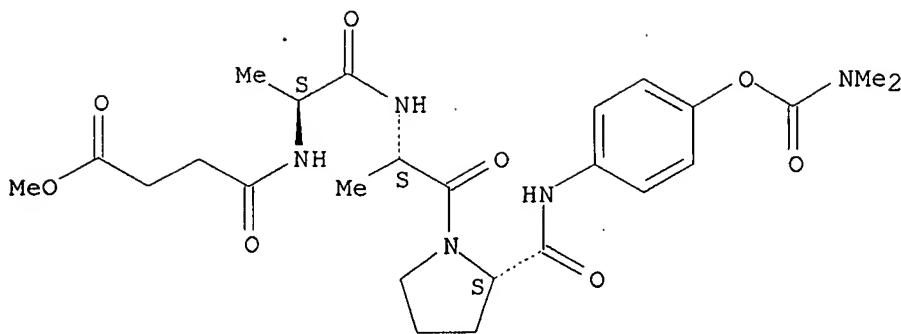
Absolute stereochemistry.



RN 92279-28-2 CAPLUS

CN L-Prolinamide, N-(4-methoxy-1,4-dioxobutyl)-L-alanyl-L-alanyl-N-[4-  
[(dimethylamino)carbonyl]oxy]phenyl- (9CI) (CA INDEX NAME)

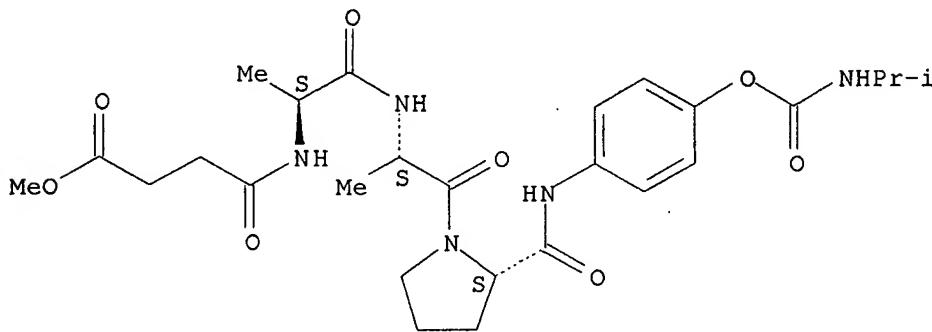
Absolute stereochemistry.



RN 92279-29-3 CAPLUS

CN L-Prolinamide, N-(4-methoxy-1,4-dioxobutyl)-L-alanyl-L-alanyl-N-[4-[(1-methylethyl)amino]carbonyl]oxy]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 92279-30-6 CAPLUS

CN L-Prolinamide, N-(4-methoxy-1,4-dioxobutyl)-L-alanyl-L-alanyl-N-[2-[(phenylamino)carbonyl]oxy]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

